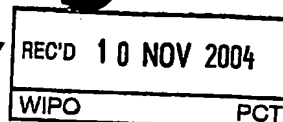


# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Article 36 and Rule 70)





Applicant's or agent's file reference 100848-1 WO	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA416)	
International application No. PCT/SE 03/01534	International filing date (day/month/year) 02.10.2003	Priority date (day/month/year) 03.10.2002
International Patent Classification (IPC) or both national classification and IPC C07D223/16		
Applicant ASTRAZENECA AB et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
  - ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:
  - I ☒ Basis of the opinion
  - II ☐ Priority
  - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV ☐ Lack of unity of invention
  - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI ☐ Certain documents cited
  - VII ☐ Certain defects in the international application
  - VIII ☐ Certain observations on the international application

Date of submission of the demand  20.04.2004	Date of completion of this report  09.11.2004
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Kollmannsberger, M Telephone No. +49 89 2399-7364 

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. **PCT/SE 03/01534**

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17):*

**Description, Pages**

1-167 as originally filed

**Claims, Numbers**

1-30 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

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EXAMINATION REPORT**

International application No. **PCT/SE 03/01534**

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☐ claims Nos.

because:

- ☒ the said international application, or the said claims Nos. 27-29 relate to the following subject matter which does not require an international preliminary examination (specify):

**see separate sheet**

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-30(in part) are so unclear that no meaningful opinion could be formed (*specify*):

**see separate sheet**

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-30
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-30
Industrial applicability (IA)	Yes: Claims	1-26,30
	No: Claims	

2. Citations and explanations

**see separate sheet**

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**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

III-1. Claims 27-29 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

III-2. Claim 1 and the dependent claims define the ring member X I. a. as being "C". It is thus unclear (Art. 6 PCT) whether a CH<sub>2</sub> group, substituted CH<sub>2</sub> groups or e. g. carbonyl groups are intended to be covered by this definition. For the purpose of the following preliminary examination this definition has been read as "CH<sub>2</sub>". Other parts are not covered by the examination report.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

**V-1. Prior art**

The following documents have been cited:

D1: WO 98 28268 A2

D2: WO 01 72324 A1

D3: WO 99 67220 A1

**V-2. Novelty (Art. 33(2) PCT):**

The claims are novel over D2 because no aryl/heteroaryl substituent in  $\alpha$ -position to the amino side chain is present in the compounds disclosed in D2. D1 discloses a generic formula (see claim 1) which includes the present claims. However, since neither any of

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the specifically disclosed example compounds nor any preferred subrange specifies the presence of an aromatic/heteroaromatic substituent in  $\alpha$ -position to the amino side chain the present claims are considered as a novel selection thereof. The same applies for D3.

The claims are thus novel over the cited prior art.

**V-3. Inventive step (Art. 33(3) PCT):**

The present application deals with compounds which inhibit the production of amyloid  $\beta$ -protein and are thus useful in the treatment of Alzheimer and related diseases. D1 is considered as the closest state of the art since it also deals with compounds having this activity. The problem to be solved in view of D1 would thus be the provision of further compounds useful for this purpose. The present claims are generically covered by the disclosure of D1 (cf. above). Additionally, D1 discloses compounds which differ from the present claims only in the absence of the aryl moiety in  $\alpha$ -position to the amino side chain (see e. g. table 6-3 on page 113) on the one hand and compounds which have such an aryl substituent but differ in that the central ring is 6-membered instead of 7-membered (see e. g. compound 5-42 in table 5-1 on page 111). The present claims must thus be seen as an obvious alternative of the compounds explicitly disclosed in D1.

Therefore, the problem to be solved by the present application must be seen in the provision of compounds presenting unexpectedly improved properties compared to the structurally closest ones disclosed in D1. Since no test data are on file, it cannot be judged whether such a problem has been solved.

The claims do not fulfil Art. 33(3) PCT.